

What Is Claimed Is:

1. A herpes viral mutant comprising:
 - (a) a deletion or inactivating mutation in both copies of the gene encoding γ 34.5; and
 - (b) an insertion of at least one copy of the γ 34.5 gene under the transcriptional control of a cell-specific and/or tumor-specific promoter.
2. The herpes viral mutant of claim 1, wherein said herpes virus is herpes simplex virus type 1.
3. The herpes viral mutant of claim 1, wherein said herpes virus is herpes simplex virus type 2.
4. The herpes viral mutant of claim 1, further comprising at least one additional endogenous deletion or inactivating mutation of a herpes viral gene.
5. The herpes viral mutant of claim 2, further comprising at least one additional endogenous deletion or inactivating mutation of a herpes viral gene.
- 15 6. The herpes viral mutant of claim 5, wherein said endogenous deletion or inactivating mutation of a herpes viral gene is a the gene that encodes ribonucleotide reductase (RR), thymidine kinase (TK), uracil DNA glycosylase (UNG), or dUTPase.
- 20 7. The herpes viral mutant of claim 5, further comprising a transgene whose product is cytotoxic to neoplastic cells.

8. The herpes viral mutant of claim 7, wherein said transgene encodes a product capable of activating or enhancing a chemotherapeutic agent, a cytokine gene, a tumor suppressor gene, or a tumoricidal gene selected from the group consisting of diphteria toxin, pseudomonas toxin, anti-angiogenesis genes, tumor vaccination genes, radiosensitivity genes, antisense RNA, or ribozymes.

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9. The herpes viral mutant of claim 8, wherein said transgene is inserted in the original γ 34.5 deletion or anywhere in the herpes UL40 locus.

10. The herpes viral mutant of claim 8, wherein said transgene encodes a suicide gene that activates a chemotherapeutic agent.

11. The herpes viral mutant of claim 10, wherein said suicide gene is mammalian cytochrome P450.

12. The herpes viral mutant of claim 11, wherein said mammalian cytochrome P450 is P450 2B1, P450 2B6, P450 2A6, P450 2C6, P450 2C8, P450 2C9, P450 2C11, or P450 3A4.

13. The herpes viral mutant of claim 2, wherein said tumor-specific promoter is derived from a gene that encodes DF3 (MUC1), AFP, CEA, PSA, tyrosinase, B-myb, or c-erbB2.

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14. The herpes viral mutant of claim 13, wherein said tumor-specific promoter is derived from the gene that encodes B-myb.

15. The herpes viral mutant Myb34.5.

16. The herpes viral mutant of claim 2, wherein said cell-specific promoter is endothelial nitric oxide synthase (eNOS) promoter expressed in endothelial cells; vascular endothelial growth factor (VEGF) receptor (flk1) promoter expressed in endothelial cells; insulin promoter expressed in beta cells of the pancreas; promoter of gonadotropin-releasing hormone receptor gene expressed in cells of the hypothalamus; matrix metalloproteinase 9 promoter, expressed in osteoclasts and keratinocytes; promoter of parathyroid hormone receptor expressed in bone cells; or dopamine beta-hydroxylase promoter expressed in noradrenergic neurons.

17. A method for selectively killing neoplastic cells that overexpress a known tumor-specific protein using a herpes viral mutant, comprising: infecting said neoplastic cells with said herpes viral mutant, said viral mutant comprising:

- (a) a deletion or inactivating mutation in a gene encoding γ 34.5; and
 - (b) an insertion of at least one copy of said γ 34.5 gene under the transcriptional control of the promoter of said tumor-specific protein, such that said promoter drives expression of said γ 34.5 gene; and
- selectively killing said neoplastic cells.

18. The method of claim 17, wherein said neoplastic cells are nervous system neoplastic cells.

19. The method of claim 18, wherein said nervous system neoplastic cells are central nervous system neoplastic cells.

20. The method of claim 17, wherein said neoplastic cells are peripheral neoplastic cells.

21. The method of claim 20, wherein said peripheral neoplastic cells are metastatic colon cells.

22. The method of claim 17, wherein said herpes viral mutant further comprises at least one additional endogenous deletion or inactivating mutation of a herpes viral gene.

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23. The method of claim 22, wherein said additional endogenous deletion or inactivating mutation of a herpes viral gene is in a gene that encodes ribonucleotide reductase (RR), thymidine kinase (TK), uracil DNA glycosylase (UNG), or dUTPase.

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24. The method of claim 17, wherein said viral mutant is Myb34.5.

25. The method of claim 17, wherein said viral mutant further comprises a suicide gene that activates a chemotherapeutic agent, and said method further comprises administering said chemotherapeutic agent.

26. The method of claim 25, wherein said suicide gene encodes cytochrome P450.

27. The method of claim 26, wherein said cytochrome P450 is selected from the group consisting of P450 2B1, P450 2B6, P450 2A6, P450 2C6, P450 2C8, P450 2C9, P450 2C11, and P450 3A4.

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28. The method of claim 27, wherein said cytochrome P450 is P450 2B1.

29. The method of claim 26, wherein said chemotherapeutic agent is cyclophosphamide or ifosfamide.

30. The method of claim 17, wherein said tumor-specific promoter in said herpes viral mutant is derived from a gene that encodes DF3 (MUC1), AFP, CEA, PSA, tyrosinase, B-*myb*, or c-*erbB2*.

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31. The method of claim 30, wherein said tumor-specific promoter in said herpes viral mutant is derived from the gene that encodes B-*myb*.

32. The method of claim 31, where said herpes viral mutant is Myb34.5.

33. A method for selectively eliminating a target cell population that overexpresses a known cell-specific protein using a herpes viral mutant, comprising:

infecting said target cells with said herpes viral mutant, said viral mutant comprising:

(a) a deletion or inactivating mutation in a gene encoding γ34.5; and

(b) an insertion of at least one copy of said γ34.5 gene under the transcriptional control of the promoter of said cell-specific protein, such that said promoter drives expression of said γ34.5 gene; and

selectively eliminating a target cell population.

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34. The method of claim 33, wherein said herpes viral mutant further comprises at least one additional endogenous deletion or inactivating mutation of a herpes viral gene.

35. The method of claim 34, wherein said additional endogenous deletion or inactivating mutation of a herpes viral gene is in a gene that encodes ribonucleotide reductase (RR), thymidine kinase (TK), uracil DNA glycosylase (UNG), or dUTPase.

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36. The method of claim 33, wherein said promoter of said cell-specific protein is: endothelial nitric oxide synthase (eNOS) promoter expressed in endothelial cells; vascular endothelial growth factor (VEGF) receptor (flk1) promoter expressed in endothelial cells; insulin promoter expressed in beta cells of the pancreas; promoter of gonadotropin-releasing hormone receptor gene expressed in cells of the hypothalamus; matrix metalloproteinase 9 promoter expressed in osteoclasts and keratinocytes; promoter of parathyroid hormone receptor expressed in bone cells; or dopamine beta-hydroxylase promoter expressed in noradrenergic neurons.

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